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Burton Rodney	B Q Rodney	Jan. 31, 2006
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ULLAH ET AL.

APPLICATION NO: 09/824,364

FILED: April 2, 2001

FOR: PHARMACEUTICAL COMPOSITION CONTAINING A COMBINATION OF A STATIN AND ASPIRIN AND METHOD

Art Unit: 1617

Examiner: Edward J. Webman

Mail Stop Appeal Brief - Patents
Commissioner for Patents
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APPEAL BRIEF

Sir:

This is an appeal from the Final Office Action mailed December 23, 2003 where Claims 28 and 36 to 40 and 42 to 47 of the above-identified application are finally rejected.

(1) REAL PARTY IN INTEREST

The real party in interest in this appeal is Bristol-Myers Squibb Company, a Delaware corporation, having a place of business at Lawrenceville-Princeton Road, Princeton, NJ 08543-4000. Bristol-Myers Squibb Company is the assignee and owner of the entire interest in the above-identified application by virtue of an assignment filed in application Serial No. 09/040,794, now U.S. Patent No. 6,235,311, and a parent of the subject application, and which was recorded in the United States Patent and Trademark Office on March 18, 1998 at Reel/Frame 9055/0943 (copy of the Notice of Recordation of Assignment being enclosed herewith).

(2) RELATED APPEALS AND INTERFERENCES

The undersigned knows of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(2A) RELATED PATENTS

U.S. Patent No. 6,235,311 to Ullah et al. is a parent of the subject application on appeal and claims a bilayered tablet wherein aspirin is present in a first layer and a statin is present in a second layer, and wherein the tablet is formulated to reduce interaction between the statin and aspirin.

The subject application on appeal is a division of U.S. application Serial No. 09/040,794, now U.S. Patent No. 6,235,311.

(3) STATUS OF CLAIMS

Claims 36, 38 to 40 and 42 to 47 have been finally rejected and are under appeal.

(4) STATUS OF AMENDMENTS

The Claims on appeal have been amended after final rejection in an Amendment After Final Rejection filed herewith.

Claims 28 and 37 have been cancelled since the subject matter of Claims 28 and 37 is covered in Claim 46.

Claim 40 has been amended to change its dependency from cancelled Claim 28 to Claim 46.

Claim 36 has been amended to correct a minor grammatical error namely, that "coating" should be "coated".

The attached "Claims on Appeal" reflect the above-described amendments.

(5) SUMMARY OF CLAIMED SUBJECT MATTER

Appellants' invention as defined in Claim 46 (the only independent claim present) is directed to a method for lowering serum cholesterol or inhibiting or treating atherosclerosis or reducing risk of or treating a cardiovascular event or disease, coronary artery disease or cerebrovascular disease, which method includes the step of administering to a patient in need of treatment a therapeutically effective amount of a pharmaceutical composition formed of a combination of a statin cholesterol lowering agent and aspirin in a single dosage form, which dosage form reduces interaction between the statin and the aspirin, and wherein the pharmaceutical composition is in the form of a tablet or capsule containing both aspirin granules and statin granules.

Claim 36 depends from Claim 46 and defines the aspirin as being in the form of enteric coated granules.

Claim 38 depends from Claim 36 and defines the enteric coated aspirin granules as including a finishing overcoat.

Claim 39 depends from Claim 38 and defines the coated aspirin granules and statin granules contained in the same capsule shells.

Claim 40 depends from Claim 46 and defines each of the aspirin and statin as being in the form of enteric coated granules.

Claim 42 depends from Claim 46 and defines the statin as being in the form of enteric coated granules.

Claim 43 depends from Claim 46 and defines the statin granules as including an outer protective coating to protect against interaction with the aspirin.

Claim 44 depends from Claim 46 and defines the pharmaceutical composition as including an antioxidant.

Claim 45 depends from Claim 44 and defines the antioxidant as vitamin C and/or vitamin E.

It is submitted that Appellants' invention as claimed is patentable over all cited references each taken alone or in any combination.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Appellants' method as defined in Claims 36, 38 to 40 and 42 to 47 is finally rejected over Eisman et al. (H1286) in view of Eichel et al. (U.S. Patent No. 5,238,686), Hodges et al. (U.S. Patent No. 5,225,202) and Shell et al. (U.S. Patent No. 5,972,389).

(7) ARGUMENT

Obviousness under 35 U.S.C. §103

A determination of obviousness under 35 U.S.C. §103 is a legal conclusion based upon factual evidence. The factual inquiries on which the conclusion is based are those defined in Graham v. John Deere Co., 383 U.S. 1 (1966), and restated in Hybritech, Inc. v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), cert. den. 107 S. Ct. 1606 (1987). These factual inquiries are:

(1) determining the scope and content of the prior art;

(2) ascertaining the differences between the invention and the prior art and the claims at issue, and

(3) resolving the level of ordinary skill in the pertinent art.

Obviousness is tested by what the combined teachings of the prior art references would have suggested to those of ordinary skill in the art, not by whether it might have been "obvious to try" a particular combination of elements from the prior art (In re Fine, 5 U.S.P.Q. 2d 1596 (Fed. Cir. 1988); In re Wiggins, 158 U.S.P.Q. 199 (1968); In re Mercier, 185 U.S.P.Q. 774 (1976); In re Antoine, 195 U.S.P.Q. 6 (1977); In re Goodwin, Margrave and Wagner, 198 U.S.P.Q. 1 (1978); In re Yates, 211 U.S.P.Q. 1149 (1981)). The teachings of the prior art can only be combined if there is some suggestion or incentive in the prior art to do so (ACS Hospital Systems, Inc. v. Montefiore Hosp. et al., 221 U.S.P.Q. 929 (CAFC 1984)).

Further, as stated in W.L. Gore & Assoc., Inc. v. Garlock, Inc., 220 U.S.P.Q. 303 (Fed. Cir. 1984):

> To imbue one of ordinary skill in the art with knowledge of the invention . . . , when no prior art reference or references . . . convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Applying the above law, it will be seen that Appellants' invention as claimed in Claims 36, 38 to 40 and 42 to 47 is patentable over the cited references each taken alone or in combination.

The use of aspirin for reducing the risk of a myocardial infarction and the use of statins for lowering cholesterol and preventing or treating atherosclerosis and cardiovascular disease and cerebrovascular disease are known in the art. In fact, it is not uncommon that patients having elevated cholesterol levels who are at high risk for a myocardial infarction take both a statin and aspirin. However, use of both a statin and aspirin in a single dosage form could result in drug interaction, which could result in physical and chemical incompatibility, leading to a reduction in benefit derived from these drugs. Accordingly, in the past, patients on both statin and aspirin have taken these drugs in separate dosage forms.

With regard to possible drug interaction, aspirin is an acid, while some of the statins, such as pravastatin, atorvastatin and cerivastatin, are alkali salts. Thus, mixing of such statins (alkali salts) with aspirin could result in aspirin hydrolysis as well as statin degradation. Pravastatin, on the other hand, is also a very acid labile compound. When pravastatin and aspirin are combined, the aspirin could cause pravastatin degradation which could result in lower bioavailability of pravastatin. Accordingly, statins and aspirin, until now, have not been formulated together in a single dosage form.

In accordance with the present invention, a method is defined in Claim 46 for lowering serum cholesterol, preventing or inhibiting or treating atherosclerosis, and/or reducing risk of or treating a cardiovascular event or disease including coronary artery disease and cerebrovascular

disease, wherein a pharmaceutical composition containing a combination of a statin cholesterol lowering agent and aspirin in a single dosage form, in a manner so as to minimize interaction of the statin and aspirin and thus minimize physical and chemical incompatibility, is administered to a patient in need of treatment.

It is submitted that Appellants' method which employs a combination of a statin cholesterol lowering agent and aspirin in a single dosage form, which dosage form reduces interaction between the statin and the aspirin, and is in the form of a tablet or capsule, is patentable over Eisman et al. in view of Eichel et al., Hodges et al. and Shell et al.

All of the claims on appeal are rejected under 35 U.S.C. §103(a) as being unpatentable over Eisman et al. taken in view of Eichel et al., Hodges et al. and Shell et al.

It should be pointed out that the subject application on appeal is a divisional of application Serial No. 09/040,794 now U.S. Patent No. 6,235,311 (hereinafter the '311 patent) in which Claim 1 defines

> "a pharmaceutical composition comprising a statin cholesterol lowering agent and aspirin in a formulation to reduce statin:aspirin interaction wherein the statin and aspirin are formulated together in a bilayered tablet, the aspirin being present in a first layer, and the statin being present in a second layer."

The present claims on appeal define a method of treatment employing a single dosage form which is a tablet or capsule containing both aspirin granules and statin granules, which dosage form reduces interaction between the statin and aspirin.

The only difference between the single dosage form employed in the method of treatment claimed in the subject application on appeal and the pharmaceutical composition claimed in the '311 patent is that in the '311 patent a bilayered tablet is claimed whereas in the present method claims on appeal a single dosage form which is a tablet or capsule is claimed.

In the '311 patent, the Examiner cited, among others, Eisman et al. H1286 and Hodges et al. U.S. Patent No. 5,225,202, both of which are also cited against the claims on appeal. It will be seen hereinafter that the Eichel et al. and Shell et al. patents which are also cited in the present application, in addition to Eisman et al. and Hodges et al., add little or nothing to Eisman et al. and Hodges et al. which would make Appellants' method as claimed obvious. Thus, it is submitted that Appellants' method as claimed is patentable for the same reasons that pharmaceutical composition claimed in the '311 patent is patentable.

With regard to the rejection under 35 U.S.C. §103(a) of the claims of this application as being unpatentable over Eisman et al. in view of Eichel et al., Hodges et al., and Shell et al., the Examiner maintains that:

"Eisman et al teach a method of lowering cholesterol by administration of a combination of an HMG CoA reductase inhibitor and a pharmaceutical which reduces cholesterol other than by inhibiting HMG CoA reductase (abstract). Lovastastin (column 8 lines 56-59) and aspirin (column 13 line 42) are disclosed. Tablets and capsules are disclosed (column 15 line 10). Antioxidants such as ascorbic acid are disclosed (column 15 line 14).

Eichel et al., teach sustained release preparations of aspirin wherein the aspirin is uncoated as well as coated with an enteric coat (abstract). Granular drugs are specified (column 5 line 65).

Hodges et al., teach enteric-coated pellets (abstract). Pravastatin is specified (table, column 5).

Shell et al teach a plurality of drugs carried by particulates, wherein each particulate carries one drug, to vary the release of each drug according to its half-life by varying the release rate of the particles carrying each drug and/or the number of particles carrying the drug (column 4 line 48 column 10 line 4)."

The Examiner concludes that:

"It would have been obvious to one of ordinary skill to deliver the composition of Eisman et al. with the vehicle of Eichel et al., to achieve the beneficial effect of controlled release. As to coating statins as well, Hodges et al. teach such.

It would have been further obvious to one of ordinary skill to place the two drugs of Eisman et al in separate particulates to achieve the beneficial effect of varying release individually according to half-life in view of Shell et al.

Applicants argue that Eisman et al. do not teach a Statin and Aspirin. However, as stated in the description above, Eisman et al. does so teach.

Applicants argue that neither secondary reference teaches applicants combination of drugs. However, again the primary reference does so teach."

Eisman et al. disclose a method for treating peripheral atherosclerotic disease employing a cholesterol lowering drug such as an HMG CoA reductase inhibitor and optionally a pharmaceutical which reduces serum cholesterol by a mechanism other than inhibiting production of the enzyme HMG CoA reductase.

Examples of HMG CoA reductase inhibitors disclosed by Eisman et al. include the statins pravastatin and lovastatin.

Examples of the pharmaceutical which functions other than by inhibiting the enzyme HMG CoA reductase include ACE inhibitors, squalene synthetase inhibitors, fibrates and aspirin, among many others.

The Examiner refers to Column 15, line 10 of Eisman et al. as disclosing tablets.

In Column 15 starting at line 5, it is indicated that "the combination of the cholesterol lowering drug and/or ACE inhibitor . . . may be incorporated in a conventional dosage form, such as a tablet, capsule, elixir or injectable." Eisman et al. also teach various other combinations of cholesterol lowering drugs including statins and squalene synthetase inhibitors or fibrates in the same dosage form. However, Eisman et al. do not disclose or suggest employing a statin and aspirin in the same dosage form.

There is no teaching, disclosure or suggestion in Eisman et al. of a method of treating a cardiovascular disease or event with a tablet or capsule containing a cholesterol lowering agent and aspirin. Eisman et al. teach tablets or capsules containing a statin cholesterol lowering drug and an ACE inhibitor or squalene synthetase inhibitor or fibrate. There is no teaching or suggestion of any dosage form containing a cholesterol lowering drug and aspirin. One skilled in the art reading Eisman et al. would surmise that aspirin and a statin could interact in the same dosage form and thus would employ each in separate dosage forms.

The essence of Appellants' invention as claimed is defined as a method of treatment which includes the step of administering a combination of a statin cholesterol lowering agent and aspirin in a single dosage form, which is a tablet or capsule, which dosage form reduces interaction between the statin and aspirin.

Eisman et al. do not disclose or suggest a single dosage form containing both a statin and aspirin. Eisman et al. do not disclose or give the slightest hint as to how to prevent or reduce interaction between a statin and aspirin in a single dosage form. At best, one skilled in the art reading Eisman et al., knowing that a statin and aspirin unfavorably interact, absent the use of hindsight in view of Appellants' disclosure, would employ the statin and aspirin in separate dosage forms.

There is no disclosure or suggestion of Appellants' method as claimed in Eisman et al. In view of the foregoing, it is clear that Appellants' invention as claimed in Claims 36, 38 to 40 and 42 to 47 is patentable over Eisman et al. taken alone.

Eichel et al. disclose a sustained-release formulation containing a core containing a water-soluble drug, such as aspirin, an inner wall microencapsular control coating, and an outer wall enteric coating. The coated aspirin may be placed in either capsules or tablets.

There is no disclosure or suggestion in Eichel et al. of use of a combination of a cholesterol lowering drug and aspirin as employed in Appellants' method. Eichel et al. only discloses coated aspirin, and does not disclose or suggest lowering cholesterol or treating a cardiovascular disease or event employing a tablet or capsule containing a combination of a cholesterol lowering drug and aspirin.

Eichel et al. does not address the problem of reducing interaction of a statin and aspirin in a single dosage form.

In view of the above, it is clear that Appellants' method as claimed in Claims 36, 38 to 40 and 42 to 47 is patentable over Eichel et al. taken above.

Hodges et al. disclose an enteric coated formulation which may contain pravastatin and may be in the form of a pellet or tablet.

Hodges et al. do not disclose or suggest use of a combination of a cholesterol lowering drug and aspirin, let alone in a single dosage form as claimed in the method of the present invention. Hodges et al. makes no disclosure or suggestion as to how to reduce interaction between a statin and aspirin in a single dosage form.

Accordingly, Hodges et al. is devoid of any teaching or suggestion of Appellants' inventive concept, namely, a method for lowering cholesterol or inhibiting or treating a cardiovascular disease or event employing a combination of a statin cholesterol lowering drug and aspirin in a single dosage from, which is designed to reduce interaction between the statin and aspirin. Thus, it is clear that Appellants' method as claimed in Claims 36, 38 to 40, and 42 to 47 is patentable over Hodges et al. taken alone.

U.S. Patent No. 5,972,389 to Shell et al. discloses controlled release oral drug dosage forms in the form of a tablet or capsule containing drug particles dispersed in a swellable/erodible polymer. In Column 9 starting at line 48 continuing to Column 10, line 4, it is disclosed that particles of two or more drugs may be co-administered in one medication unit by employing a plurality of drug-containing particles, some of the particles containing a first drug/polymer composition designed to release the first drug at its ideal rate and duration, while other particles contain a second drug/polymer composition designed to release the second drug at its ideal rate and duration. In Column 6, line 20, lovastatin is disclosed as a useful drug for the Shell et al. formulation.

There is no disclosure or suggestion in Shell et al. of employing a statin and aspirin in a single dosage form in a manner to prevent interaction between them as employed in Appellants' method as claimed. Shell et al. relates to a controlled release composition employing special polymers and is not concerned with using a statin and aspirin in the same dosage form. Appellants' method employs a single dosage formulation containing a statin and aspirin in a manner to reduce interaction between them. Appellants' method as claimed is totally different from and is not suggested or made obvious by Shell et al. In fact, Shell et al. has nothing whatsoever to do with Appellants' method as claimed which employs a single dosage form containing a statin and aspirin.

Accordingly, it is clear that Appellants' method as claimed is patentable over Shell et al. taken alone.

It is also submitted that Appellants' method as claimed is patentable over a combination of Eisman et al. taken in view of Eichel et al., Hodges et al., and Shell et al.

Eisman et al. does not disclose or suggest a single dosage form such as a tablet or capsule containing a combination of a cholesterol lowering drug and aspirin as required in Appellants' method. Eisman et al. only disclose tablets or capsules containing a statin cholesterol lowering drug and an ACE inhibitor or a fibrate or a squalene synthetase inhibitor. Eisman et al. disclose aspirin but does not disclose or suggest aspirin in a single dosage form with a statin or how to reduce interaction between the statin and aspirin. At best, one skilled in the art reading Eisman et al. would employ the statin and aspirin in separate dosage forms in view of the expected interaction between them.

Eichel et al. only discloses coated aspirin and does not disclose or suggest a combination of aspirin and a cholesterol lowering drug in a single dosage form as employed in Appellants' method.

There is no disclosure or suggestion in Eisman et al. or Eichel et al. that the Eichel et al. coated aspirin, or any aspirin for that matter, should be employed together with a statin cholesterol lowering drug in a single dosage form as employed in Appellants' method. There is no disclosure or suggestion in Eichel et al. that the Eichel et al. coating for the aspirin would inhibit the aspirin from interacting with a statin if both were employed in the same dosage form. The use of a coating for aspirin so that it can be employed in a sustained release formulation does not make it obvious to employ such coated aspirin to prevent or reduce interaction with a statin.

There is no disclosure or suggestion in Eisman et al., Eichel et al., Hodges et al. and Shell et al. that the Hodges et al. coated pravastatin or the Shell et al. coated lovastatin should be employed by one skilled in the art together with aspirin in a single dosage form. There is nothing in Hodges et al. or Shell et al. which would suggest that the coatings for the statin would reduce interacting with aspirin when each is employed together in a single dosage form. Thus, the secondary references add nothing to Eisman et al. which would make Appellants' method obvious.

Shell et al. has nothing to do with a single dosage form containing aspirin and a statin as employed in Appellants' method. At best, Shell et al. discloses use of lovastatin in a formulation with another drug; however, there is no disclosure or suggestion that such other drug could be aspirin or that the polymer of Shell et al. could prevent or reduce interaction between aspirin and statin. Thus, Shell et al. adds nothing to the combination of references which would make Appellants' method obvious.

Eisman et al. actually teaches away from employing a statin and aspirin in a single dosage form. Although Eisman et al. disclose aspirin as an example of a "pharmaceutical or other serum cholesterol lowering agent . . .", Eisman et al. does not disclose or suggest that aspirin should be employed in the same dosage form with a statin. Eisman et al. specifically discloses many combinations of a statin and other pharmaceutical for use in the same dosage form, namely, ACE inhibitors, fibrates and squalene synthetase inhibitors (see Column 15 starting at line 5 to line 11 and lines 60 to 63 and Examples 4 and 5, 6 to 8, 9, 10, 13, 14, 15, 16, 17 to 19, 22 and 23, 24 and 26). As seen, Eisman et al. disclose dozens and dozens of combinations of cholesterol lowering drugs employed in a single dosage form, none of which includes a combination with aspirin in a single dosage form. Thus, one skilled in the art reading Eisman et al. could only conclude that the statin and aspirin are not to be employed in the same dosage form.

The secondary references teach coated aspirin for sustained release delivery and coated statin for sustained release delivery. Absent the use of hindsight in view of Appellants' disclosure, one skilled in the art reading the secondary references and Eisman et al. would not be motivated to combine a statin and aspirin in a single dosage form since none of these references discloses or suggests how this could be accomplished while reducing interaction between them. In fact, one skilled in the art reading Eisman et al. would be discouraged from making such a single dosage form for the reasons set out above.

There is no disclosure or suggestion in the combination of all cited references of a method for lowering cholesterol or inhibiting or treating cardiovascular disease or event employing a combination of a cholesterol lowering drug and aspirin in the same tablet or capsule in a manner to inhibit interaction between the cholesterol lowering drug and the aspirin.

In view of the foregoing, it is clear that Appellants' method as claimed which employs a combination of a cholesterol lowering drug and aspirin in the same dosage form which dosage form reduces interaction between the cholesterol lowering drug and aspirin is patentable over a combination of Eisman et al. taken with Eichel et al., Hodges et al. and Shell et al.

The present situation with regard to lack of teaching in the cited references of how to make the single dosage form employed in the method of the invention is not unlike where the cited prior art names a compound but where no known or obvious method exists for making that compound and thus the cited prior art will not place the compound in the possession of the public. In re Hoeksema, 158 U.S.P.Q. 596 (CCPA 1968). A compound is not obvious if there is no known way or obvious way to prepare it. In re Hoeksema et al., supra. By the same token, a formulation or a method using such formulation is not obvious if there is no known way to prepare it. It is Appellants' contention that the cited prior art taken alone or in any combination does not disclose or suggest

Appellants' method as claimed which employs a single dosage form containing a statin and aspirin in a manner to reduce interaction between the statin and aspirin, and therefore does not place Appellants' method which employs the formulation in the public.

The Examiner has not established a prima facie case of obviousness. The cited references taken in combination do not disclose or suggest a method employing a single formulation containing a statin and aspirin in a manner to reduce interaction between them. That this is apparent can be seen from the fact that none of the cited references even relates to a single dosage form containing both aspirin and a statin; Eisman et al. does not teach or suggest a single dosage form containing both a statin and aspirin as claimed herein. In addition, the cited references taken in combination do not teach how to make a single formulation containing both a statin and aspirin in a manner to prevent interaction between them. In determining patentability of a method of use which employs a drug formulation, it is appropriate to consider the manner of preparation of the formulation versus the prior art; if there is no disclosure of how to make it, it cannot be considered in the possession of the public. In re Hoeksema et al., supra. There is no disclosure in the cited art of how to make a single formulation (as employed in Appellants' method as claimed) containing both a statin and aspirin in a manner to prevent interaction between them as explained hereinbefore.

In view of the above, it is clear that the Examiner has not cited any references taken singly or in combination which would make Appellants' method obvious.

It is also submitted that the very combination of Eisman et al. taken in view of Eichel et al., Hodges et al. and Shell et al. is improper as lacking any foundation and could only be made with the use of hindsight in view of Appellants' disclosure. The cited prior art does not provide motivation or a suggestion or basis for modifying Eisman et al. in view of Eichel et al., Hodges et al. and Shell et al.

The Eichel et al., Hodges et al. and Shell et al. patents do not disclose or suggest that a statin should be employed in a single dosage form with aspirin. Eisman et al. do not teach or suggest a single dosage form containing both a statin and aspirin since it was known that the statin and aspirin would interact to reduce efficacy of each. At best, Eisman et al. discloses use of a statin and aspirin in separate dosage forms.

Even if the combination of references were made, it still would not disclose or make obvious Appellants' method which employs a single dosage form containing aspirin and a statin since none of the cited references taken alone or in any combination teaches or suggests any single composition containing aspirin and a statin in a manner to reduce interaction between them.

(7A) SUMMARY OF ARGUMENTS

Summing up, it is submitted that Appellants' invention as claimed is patentable over a combination of Eisman et al., taken in view of Eichel et al., Hodges et al. and Shell et al. Even if the techniques of the cited references were combined, the combination would not disclose or suggest to one skilled in the art reading the cited references how to make a single dosage form containing a statin and aspirin in a manner to reduce interaction between them (as employed in Appellants' method as claimed). Accordingly, it is submitted that the cited combination of references are no more relevant than each taken alone and do not make Appellants' method employing the single dosage form as claimed obvious.

The fact that the cited references do not disclose or suggest a procedure for preparing a single dosage form containing a statin and aspirin in a manner to reduce interaction between them, employed in Appellants' method of use as claimed further supports Appellants' case for patentability of their method.

In applying the criteria for patentability as enunciated in Graham v. John Deere Co., supra, it is seen that:

(1) the scope of the content of the prior art has been reviewed above.

(2) the differences between the invention and the prior art have been set out, namely, that the prior art does not disclose or suggest a method of treatment employing a single dosage form containing a statin and aspirin in a manner to reduce interaction between them.

(3) the level of ordinary skill in the art is exceedingly high and involves scientists having Masters, Ph.D. and M.D. degrees.

It is submitted that there is no disclosure or suggestion in any of the cited references or combination thereof of the claimed method of use. Absent the use of hindsight in view of Appellants' disclosure, there would be no reason for one skilled in the art reading the cited references to combine these references. The use of hindsight in view of Appellants' disclosure in combining references to reject Appellants' claims is clearly improper in view of In re Pye et al., 148 U.S.P.Q. 426 (CCPA 1966), ACS Hospital Systems, Inc. v. Montefiore Hospital, supra.; and W.L. Gore & Assoc., Inc. v. Garlock, Inc.., supra.

(7B) CONCLUSION

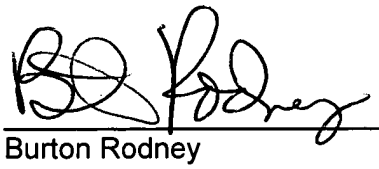
The Examiner has not established any factual basis sufficient to support the Examiner's conclusions and thus establish a prima facie case for obviousness of Appellants' invention as claimed. In re Piasecki, 745 F.2d 1468, 223 U.S.P.Q. 785 (Fed. Cir. 1984). In essence, the Examiner has merely alleged that the differences between Appellants' invention and the cited art

are obvious, but has not set forth any basis in logic or scientific principle to support such contention as required under In re Soli, 317 F.2d 941, 127 U.S.P.Q. 797 (CCPA 1963). The very combination of references is improper as being based on hindsight in view of Appellants' disclosure.

In view of the fact that Appellants' invention as defined in Claims 36, 38 to 40 and 42 to 47 of this application, is neither disclosed nor suggested in or made obvious by the cited prior art, it is submitted that Appellants have shown that their invention as claimed is not anticipated by and is clearly patentable over the cited combination of references. Therefore, it is believed that the Examiner's final rejection of the claims on appeal should be reversed and that such claims should be allowed.

Appellants hereby waive an oral hearing.

Respectfully submitted,



Burton Rodney
Attorney for Appellants
Reg. No. 22,076

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Date: Jan. 31, 2006

(8) CLAIMS APPENDIX
(CLAIMS ON APPEAL)

36. The method as defined in Claim 46 wherein the aspirin in the pharmaceutical composition administered is in the form of enteric coated granules.

38. The method as defined in Claim 36 wherein the enteric coated aspirin granules include a finishing overcoat, and the coated aspirin and the statin are in the form of a table or capsule.

39. The method as defined in Claim 38 wherein the coated aspirin granules and the statin in the form of granules are contained in the same capsule shells.

40. The method as defined in Claim 46 wherein in the pharmaceutical composition administered the aspirin is in the form of enteric coated granules of aspirin and the statin is in the form of enteric coated granules of statin, in the form of compressed tablets or capsules.

42. The method as defined in Claim 46 wherein the statin is in the form of enteric coated statin granules.

43. The method as defined in Claim 46 wherein the statin granules include an outer protective coating to protect against interaction with the aspirin.

44. The method as defined in Claim 46 wherein the pharmaceutical composition administered further includes an antioxidant.

45. The method as defined in Claim 44 wherein the antioxidant is vitamin C and/or vitamin E.

46. A method for lowering serum cholesterol or inhibiting or treating atherosclerosis or reducing risk of or treating a cardiovascular event or disease, coronary artery disease or cerebrovascular disease, which comprises administering to a patient in need of treatment a therapeutically effective amount of a pharmaceutical composition comprising a combination of a statin cholesterol lowering agent and aspirin in a single dosage form, which dosage form reduces

interaction between the statin and the aspirin, wherein the pharmaceutical composition is in the form of a tablet or capsule containing both aspirin granules and statin granules.

47. The method as defined in Claim 46 wherein the statin employed is pravastatin, lovastatin, simvastatin, atorvastatin, fluvastatin or cerivastatin.

(9) EVIDENCE APPENDIX

None.

(10) RELATED PROCEEDINGS APPENDIX

None.

HX96 US - DIV [1]

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Burton Rodney		January 31. 2006
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RE APPLICATION OF
ISMAT ULLAH, ET AL
APPLICATION NO: **09/824364**
FILED: **04/02/2001**
FOR: **PHARMACEUTICL COMPOSITION CONTAINING A COMBINATION OF A STATIN AND ASPIRIN AND METHOD.**

ART UNIT: **1616**
EXAMINER: **WEBMAN, EDWARD J**

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Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Sir:

Enclosed herewith is one copy of the Appeal Brief in the above-identified application.

☒ Please charge Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company in the amount of $500 for payment of the appeal fee. An additional copy of this paper is here enclosed. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

☐ Enclosed is a Petition for Extension of Time.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000

Burton Rodney
Attorney for Applicant
Reg. No. 22,076
Phone: 609-252-4336
Date: January 31, 2006

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Burton Rodney		January 31, 2006
Type or print name	Signature	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ULLAH ET AL.

APPLICATION NO: 09/824,364

FILED: April 2, 2001

FOR: PHARMACEUTICAL COMPOSITION CONTAINING A COMBINATION OF A STATIN AND ASPIRIN AND METHOD

Art Unit: 1617

Examiner: Edward J. Webman

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

LETTER IN RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF (37 CFR §41.37)

Sir:

This is in response to the Notification of Non-Compliant Appeal Brief (37 CFR §41.37) mailed January 6, 2006 filed in response to the Appeal Brief filed on August 2, 2004 in the above-identified application.

In the "Notification", the Examiner indicates that the Appeal Brief is defective for failure to comply with 37 CFR §41.37 in the material entitled "Obviousness under 35 USC §103 appearing in the ISSUE section should be in the ARGUMENT section."

Enclosed herewith is an Appeal Brief (original and 3 copies) wherein the material entitled "Obviousness under 35 USC §103" is included in the ARGUMENT section.

It is believed that the enclosed Appeal Brief is in compliance with 37 CFR §41.37.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Burton Rodney
Attorney for Appellants
Reg. No. 22,076

Date: Jan. 31, 2006